10

15

20

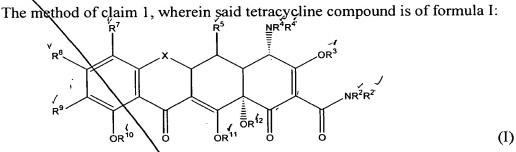
25

30

## **CLAIMS**

A method for controlling Cryptosporidium parvum in a mammal, comprising administering to said mammal an effective amount of a tetracycline compound, such that Cryptosporidium parvum is controlled in said mammal.

2.



wherein:

X is  $CHC(R^{13}Y,Y)$ ,  $CHR^{6}$ , S,  $NR^{6}$ , or O;

R<sup>2</sup>, R<sup>4</sup> and R<sup>4</sup> are each hydrogen, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, aryl, heterocyclic, heteroaromatic or a prodrug moiety:

R2', R3, R10, R11 and R12 are each hydrogen or a pro-drug moiety;

R<sup>5</sup> is hydroxy, hydrogen, thiol alkanoyl, aroyl, alkaroyl, aryl, heteroaromatic, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, or an arylalkyl;

R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup> and R<sup>9</sup> are each independently hydrogen, hydroxyl, halogen, thiol, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, or an arylalkyl;

R<sup>13</sup> is hydrogen, hydroxy, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, or an arylalkyl;

Y' and Y are each independently hydrogen, halogen, hydroxyl, cyano, sulfhydryl, amino, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkyl ulfinyl, alkylsulfonyl, alkylamino, or an arylalkyl;

and pharmaceutically acceptable salts thereof.

- The method of claim 2, wherein R<sup>2</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>10</sup>, R<sup>11</sup>, and R<sup>12</sup> are each hydrogen or a 3. prodrug moiety.
- The method of claim 2, wherein R<sup>4</sup> and R<sup>4</sup> are each alkyl. 4.





- 5. The method of claim 5, wherein R<sup>4</sup> and R<sup>4</sup> are each methyl.
- $\neq$ 6. The method of claim 2, wherein R<sup>5</sup> is alkanoyl.
- 5  $\neq$ 7. The method of claim 5, wherein  $R^5$  is an ester.
  - 8. The method of claim 7, wherein R<sup>5</sup> is a propanoic ester.
    - 9. The method of claim 2, wherein  $R^5$  is hydroxyl.
- 10  $\downarrow$  10. The method of claim 2, wherein R<sup>5</sup> is hydrogen.
  - $\chi$  11. The method of claim 2, wherein X is S.
- 15 12. The method of claim 2, wherein X is CHR<sup>6</sup>.
  - 13. The method of claim 12, wherein R<sup>6</sup> is alkyl.
  - 14. The method of claim 13, wherein R<sup>6</sup> is methyl.
- 20

  15. The method of claim 2, wherein R<sup>6</sup> comprises a heteroatom.
  - +16. The method of claim 15, wherein  $R^6$  comprises a sulfur atom.
- 25  $\neq$  17. The method of claim 16, wherein  $R^6$  is a thioether.
  - +18. The method of claim 17, wherein  $R^6$  is a cyclopentylthio ether.
  - 19. The method of claim 2, wherein R<sup>9</sup> is hydrogen.
  - 20. The method of claim 2, wherein R<sup>9</sup> is alkyl or alkenyl.
    - 21. The method of claim 20, wherein R<sup>9</sup> is cyclopentenyl.
- 35  $\nearrow$ 22. The method of claim 20, wherein  $R^9$  is t-butyl.
  - +23. The method of claim 2, wherein  $R^9$  is alkynyl.

- **∠**24.
- The method of claim 22, wherein R<sup>9</sup> is 2-cyclohexenyl-ethynyl.
- The method of claim 1, wherein said tetracycline compound is of the formula: £ 25.

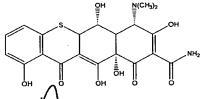
The Color of the Color of the Color of the Color

The method of claim 1, wherein said tetracycline compound is of the formula: ∠26.

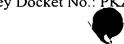
The method of claim 1, wherein said tetracycline compound is of the formula: 10 / 27.

The method of claim 1, wherein said tetracycline compound is of the formula: 28.

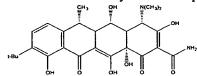
- 15
  - The method of claim 1, wherein said tetracycline compound is of the formula: × 29.



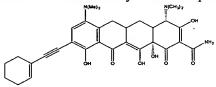
- The method of claim 1, wherein said tetracycline compound is doxycycline.
- 20



∠31. The method of claim 1, wherein said tetracycline compound is of the formula:



The method of claim 1, wherein said tetracycline compound is of the formula:



5

- 33. The method of claim 1, wherein said mammal is immunocompetent.
- 34. The method of claim 1, wherein said mammal is immunocompromised.

10

#Q

. 10

- 35. The method of claim 1, wherein said mammal is a human.
- 36. The method of claim 35, wherein said human has an immunodeficiency.
- 15 37. The method of claim 36, wherein said human has AIDS.
  - 38. The method of claim 36, wherein said human has undergone chemotherapy.
- 39. The method of claim 1, wherein said effective amount is effective to treat a 20 Cryptosporidium parvum related disorder in said mammal.
  - 40. The method of claim 37, wherein said *Cryptosporidium parvum* related disorder is diarrhea.
- 25 41. The method of claim 37, wherein said *Cryptosporidium parvum* related disorder is cryptosporidiosis.
  - 42. The method of claim 1, wherein said tetracycline compound inhibits more than 70% of Cryptosporidium parvum at a concentration less than 100 μg/ml.

30

43. The method of claim 41, wherein said tetracycline compound inhibits more than 70% of Cryptosporidium parvum at a concentration less than 10 µg/ml.

- 44. The method of claim 43, wherein said tetracycline compound inhibits more than 70% of *Cryptosporidium parvum* at a concentration less than 1 µg/ml.
- A method for treating a *Cryptosporidium parvum* related disorder in a mammal, comprising administering to said mammal an effective amount of a tetracycline compound such that said mammal is treated for said disorder.
  - 46. The method of claim 45, wherein said tetracycline compound is of formula I:



20

25

10

Gira Biri Iv II.II

$$R^{9}$$

$$QR^{10}$$

$$QR^{11}$$

$$QR^{12}$$

$$QR^{11}$$

$$QR^{12}$$

$$QR^{11}$$

$$QR^{12}$$

$$QR^{11}$$

$$QR^{12}$$

$$QR^{12}$$

$$QR^{11}$$

$$QR^{12}$$

$$QR^{12}$$

$$QR^{13}$$

$$QR^{14}$$

$$QR^{14}$$

$$QR^{15}$$

$$QR^{15$$

wherein:

X is CHC(R<sup>13</sup>Y'Y), CHR S, NR<sup>6</sup>, or O;

R<sup>2</sup>, R<sup>4</sup>, and R<sup>4</sup> are each independently hydrogen, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, arylalkyl, aryl, heterocyclic or heteroaromatic;

R<sup>2</sup>, R<sup>3</sup>, R<sup>10</sup>, R<sup>11</sup> and R<sup>12</sup> are each hydrogen or a pro-drug moiety;

R<sup>5</sup> is hydroxy, hydrogen, thiol, alkanoyl, aroyl, alkaroyl, aryl, heteroaromatic, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, or arylalkyl;

R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup> and R<sup>9</sup> are each independently hydrogen, hydroxyl, halogen, thiol, alkyl, alkenyl, alkynyl, aryl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, or arylalkyl;

R<sup>13</sup> is hydrogen, hydroxy, alkyl, alkenyl, alkynyl, alkynyl, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, or arylalkyl;

Y' and Y are each independently hydrogen, halogen, hydroxyl, cyano, sulfhydryl, amino, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, alkylamino, or arylalkyl;

 ${\tt and \'pharmaceutically} \ acceptable \ salts \ thereof.$ 

- The method of claim 46, wherein R<sup>2</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>10</sup>, R<sup>11</sup>, and R<sup>12</sup> are each hydrogen or a 47. prodrug moiety.
- The method of claim 47, wherein R<sup>4</sup> and R<sup>4</sup> are each methyl. 48.
- The method of claim 48, wherein R<sup>5</sup> is alkanoyl, an ester group, a hydroxyl group or · 49. hydrogen.
  - The method of claim 48, wherein X is S or CHR<sup>6</sup>. 50.

10

- The method of claim 50, wherein R<sup>6</sup> is alkyl. 51.
- The method of claim 50, wherein R<sup>6</sup> comprises a heteroatom. ∠<sup>52</sup>.
- The method of claim 52, wherein R<sup>6</sup> is a thioether. 15 <sub>∠</sub>53.
  - The method of claim 46, wherein R<sup>9</sup> is hydrogen, alkyl, alkenyl, or alkynyl. 54.
  - The method of claim 54, wherein R<sup>9</sup> is cyclopentenyl. 55.

The method of claim 54, wherein R<sup>9</sup> is t-butyl. ₹56.

- The method of claim 54, wherein R<sup>9</sup> is 2-cyclohexenyl-propynyl. ₹57.
  - 58. The method of claim 46, wherein said tetracycline compound is selected from the group consisting of 5-propionyl-6-eyclopentylsulfanylmethyl doxycycline; thiatetracycline; 9cyclopent-1-enyl-doxycycline; 5-propionyl-9-tert-butyl-doxycycline; doxycycline; 9-tert-butyl doxycycline; 9-cyclohex-1-enylethynyl minocycline; and 6-cyclopentylsulfanylmethyl doxycycline.
  - 59. The method of claim 46, wherein said mammal is immunocompetent.
  - The method of claim 46, wherein said mammal is immunocompromised. 60.
- 35 61. The method of claim 46, wherein said mammal is a human.
  - The method of claim 61, wherein said human is immunodeficient. 62.

20

25

30

30

- 63. The method of claim 62, wherein said human has AIDS.
- 64. The method of claim 62, wherein said human has undergone chemotherapy.
- 65. The method of claim 46, wherein said effective amount is effective to treat a *Cryptosporidium parvum* related disorder in said mammal.
- 66. The method of claim 65, wherein said *Cryptosporidium parvum* related disorder is diarrhea.
  - 67. The method of claim 65, wherein said *Cryptosporidium parvum* related disorder is cryptosporidiosis.
- 15 68. The method of claim 46, further comprising the administration of a pharmaceutically acceptable carrier.
  - 69. The method of claim 46, further comprising the administration of a supplementary anti-Cryptosporidium parvum agent.
  - 70. The method of claim 46, wherein said supplementary agent is paromomycin or a derivative thereof.
- 71. A pharmaceutical composition comprising an effective amount of a tetracycline compound to treat a *Cryptosporidium parvum* related disorder in a mammal and a pharmaceutically acceptable carrier.
  - 72. The pharmaceutical composition of claim 71, wherein said tetracycline compound is selected from the group consisting of: 5-propionyl-6-cyclopentylsulfanylmethyl doxycycline; thiatetracycline; 9-cyclopent-1-enyl-doxycycline; 5-propionyl-9-tert-butyl-doxycycline; doxycycline; 9-tert-butyl doxycycline; 9-cyclohex-1-enylethynyl minocycline; and 6-cyclopentylsulfanylmethyl doxycycline.
- 73. The pharmaceutical composition of claim 71, wherein said tetracycline compound is 9-35 cyclopent-1-enyl-doxycycline.

- 74. The pharmaceutical composition of claim 71, wherein said *Cryptosporidium parvum* related disorder is cryptosporidoisis.
- 75. The pharmaceutical composition of claim 71, wherein said *Cryptosporidium parvum* 5 related disorder is diarrhea.
  - 76. The pharmaceutical composition of claim 71, further comprising an effective amount of a supplementary anti-Cryptosporidium paryum agent.
- 10 77. A tetracycline compound of the formula:

